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# PRE-APPEAL BRIEF REQUEST FOR REVIEW

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| Applicant | : | Latta, Paul |
| App. No | : | 10/660,924 |
| Filed | : | September 12, 2003 |
| For | : | PREVENTION OF DIABETES THROUGH INDUCTION OF IMMUNOLOGICAL TOLERANCE |
| Examiner | : | Belyavskyi, Michail A. |
| Art Unit | : | 1644 |

CERTIFICATE OF MAILING

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Mail Stop: AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

August 17, 2005
(Date)

Marina L. Cardey, Reg. No. 52,950

**Mail Stop AF**
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicant requests review of the final rejection mailed on May 18, 2005 in the above-identified application. No amendments are being filed with this request.

Enclosed with this Request is a Notice of Appeal.

**REASONS FOR REQUEST**

Review of the above-identified application is requested for the following reasons:

1. The Examiner has maintained rejections of Claims 2-9 under 35 USC §112, first paragraph, as being non-enabling for a method of preventing onset of Type I diabetes in a mammal. Applicants submitted two Declarations under 37 CFR §1.132 by Dr. David Scharp mailed to the PTO on April 1, 2004 and April 29, 2005. The Declarations clearly show that diabetes was prevented in the non-obese diabetic mouse model using the method recited in the claim. Moreover, the Declarations and references submitted by Applicant establish the validity of the NOD mouse model in connection with human diabetes. Nevertheless, the Examiner has argued that the NOD mouse model is a not a predictable model of type I diabetes and therefore cannot be used to extrapolate data obtained from these mice to human.

The Examiner recognized that "[s]ubstantiating evidence may be in the form of animal tests, which constitute recognized screening procedures with clear relevance to efficacy in humans", citing *Ex parte Krepelka*, 231 U.S.P.Q. 746 and *Ex parte Maas*, 9 U.S.P.Q.2d 1746. Nevertheless, the Examiner has insisted that it is unpredictable from the *in vivo* murine data presented in the Declarations whether the method of the invention can be used in mammals including humans.

The Applicant set forth in the response to the previous Office Action mailed to the PTO on April 29, 2005, that the Examiner is applying a much stricter standard than required by law. MPEP 2107.03 establishes the following:

> Evidence does not have to be in the form of data from an art-recognized animal model for the particular disease or disease condition to which the asserted utility relates. Data from any test that the applicant reasonably correlates to the asserted utility should be evaluated substantively. Thus, an applicant may provide data generated using a particular animal model with an appropriate explanation as to why that data supports the asserted utility. The absence of a certification that the test in question is an industry-accepted model is not dispositive of whether data from an animal model is in fact relevant to the asserted utility. Thus, if one skilled in the art would accept the animal tests as being reasonably predictive of utility in humans, evidence from those tests should be considered sufficient to support the credibility of the asserted utility."

Office personnel should be careful not to find evidence unpersuasive simply because no animal model for the human disease condition had been established prior to the filing of the application. See In re Chilowsky, 229 F.2d

> 457, 461, 108 USPQ 321, 325 (CCPA 1956) ("The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it."); In re Wooddy, 331 F.2d 636, 639, 141 USPQ 518, 520 (CCPA 1964) ("It appears that no one on earth is certain as of the present whether the process claimed will operate in the manner claimed. Yet absolute certainty is not required by the law. The mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it.").

In these cases, it is important to note that the Food and Drug Administration has promulgated regulations that enable a party to conduct clinical trials for drugs used to treat life threatening and severely-debilitating illnesses, even where no alternative therapy exists. See 21 CFR 312.80-88 (1994). Implicit in these regulations is the recognition that experts qualified to evaluate the effectiveness of therapeutics can and often do find a sufficient basis to conduct clinical trials of drugs for incurable or previously untreatable illnesses. Thus, affidavit evidence from experts in the art indicating that there is a reasonable expectation of success, supported by sound reasoning, usually should be sufficient to establish that such a utility is credible.

In the present case, the Applicant provided ample support in the form of affidavit evidence from experts in the art indicating that the NOD mice is at present the standard model for studying Type I diabetes prevention and treatment. See arguments presented in the Response to Office Action mailed to the PTO on April 29, 2005, see pages 5 through 6. In addition, the Second Declaration of David Scharp under 37 CFR 1.132 established that the NOD mouse is the only animal model for human autoimmune, Type I diabetes because it is the only available model reasonably predictive of human disease.

While it is true that questions have been raised whether the NOD model is absolutely predictive of treatment of humans, such an absolute correlation with human disease is not required to support enablement. MPEP 2107.03 further provides:

> The applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use.

Therefore, using the proper standard set forth in the MPEP, the evidence provided by Applicant clearly supports that one skilled in the art would accept the NOD model as reasonably correlating to the condition in human.

The Examiner also believed that undue experimentation would be required to determine screening and testing protocols. However, as established in the Declaration of David Scharp, M.D., submitted on April 29, 2005, methods for determining whether normoglycemia is present have been exceedingly well known for many years; thus, only routine blood glucose monitoring would be required to demonstrate the efficacy of the claimed invention. Furthermore, the Applicants provided a sufficient showing in the Office Action Response mailed April 29, 2005, that screening for individuals susceptible to Type I diabetes is well-known and routine, amount of insulin-producing cells needed to be implanted to achieve normoglycemia is also well-known, as are the tests to determine whether normoglycemia is present (pages 7-8).

MPEP 2164.01(c) establishes that in order to meet the enablement requirement, one skilled in the art need only be able to discern an appropriate dosage or method of use without undue experimentation based on knowledge of compounds having similar physiological or biological activity. Here, the Specification at page 12, lines 26-30 clearly indicates that a dose of implanted insulin-producing cells to induce tolerance is one or two orders of magnitude less than a full dose of implant which provides adequate insulin production for normoglycemia. The full dose for achieving normoglycemia has been well worked out for many years. Accordingly, no difficulty would be had in obtaining the correct dose for any given individual. Accordingly, no undue experimentation would be required to practice the claimed invention.

Therefore, the rejection of Claims 2-9 as non-enabled is clearly improper.

2. The Examiner has improperly rejected Claims 2-9 for allegedly containing New Matter. Specifically, The Examainer has stated that the limitation added to Claim 2: "wherein said dose is at least one order of magnitude less than that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes" is not supported by the passages of the Specification pointed to by the Applicant.

The specification states at page 19, lines 13-19 that the dose for prevention is the same as the dose for tolerization that is discussed earlier in the specification in connection with disease treatment. At page 9, line 9-11, the specification clearly states that "[a]s for the bolus tolerizing

dose, the incremental tolerizing dose is typically one or two orders of magnitude lower than the curative dose. Thus, the specification clearly establishes that the dose for prevention of diabetes is "at least one order of magnitude less than that necessary to achieve normoglycemia in a mammal of the same species with type I diabetes." Therefore, there is clear support in the Specification as filed for Claim 2, and its rejection over "New Matter" is improper.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: August 17, 2005 By: _____

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